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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/069, 228	04/27/98	FLOWMAN	G 234/118

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/069,228	Applicant(s) Plowman et al.
	Examiner Anne Holleran	Group Art Unit 1642

Responsive to communication(s) filed on Jan. 19, 2000

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle* 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

- Claim(s) 2-5, 9, and 23-40 is/are pending in the application.
- Of the above, claim(s) _____ is/are withdrawn from consideration.
- Claim(s) _____ is/are allowed.
- Claim(s) 2-5, 9, and 23-40 is/are rejected.
- Claim(s) _____ is/are objected to.
- Claims _____ are subject to restriction or election requirement.

Application Papers

- See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- The drawing(s) filed on _____ is/are objected to by the Examiner.
- The proposed drawing correction, filed on _____ is approved disapproved.
- The specification is objected to by the Examiner.
- The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- All Some* None of the CERTIFIED copies of the priority documents have been received.
- received in Application No. (Series Code/Serial Number) _____.
- received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- Notice of References Cited, PTO-892
- Information Disclosure Statement(s), PTO-1449, Paper No(s). 5
- Interview Summary, PTO-413
- Notice of Draftsperson's Patent Drawing Review, PTO-948
- Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. This Office Action vacates the previous Office Action, mailed June 7, 2000.

Claims 2-5, 9 and 23-40 are pending and examined on the merits.

Claim Rejections Withdrawn:

2. The rejection of Claims 2-7, 9 and 23-37 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of Applicant's amendments to the claims.

3. The rejection of Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn in view of the Applicant's amendment to claim 23.

4. The rejection of Claims 9, 23, 24, 28 and 37 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, is withdrawn in view of Applicant's amendments to the claims.

5. The rejection of Claims 2-7, 9, 27-33 under 35 U.S.C. 102(e) as being anticipated by either US Patent 5,614,609 ("Ibanez et al., '609" filed 15 Nov 1994), US Patent 5,789,565 ("Ibanez et al.,'565" effective US filing date 15 Nov 1994) or US Patent 5,811,245 (Ibanez et al.,'245" effective US filing date 15 Nov 1994) is withdrawn in view of Applicant's amendments to the claims. However, these references are applied to new claims 38-40, see below.

6. The rejection of Claims 2, 3, 5-7, 9, 23, 24, and 32 under 35 U.S.C. 102(a) as being anticipated by Ryden et al (see page 30604, Ryden, M. et al., J. Biol. Chem. 271(48): 30603-30609, 1996 is withdrawn in view of Applicant's amendments to the claims.

7. The rejection of Claim 34 under 35 U.S.C. 103(a) as being unpatentable over either Ibanez et al., '609, Ibanez et al.,'565 or Ibanez et al.,'245 in view of US Patent 5,168,050 (Hammonds, Jr. et al, US Patent 5,168,050, publication date 1 Dec. 1992) is withdrawn in view of Applicant's amendments to the claims.

New Grounds of Rejection:

8. Claims 36, 38-40 are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 is vague and indefinite because of the use of an abbreviation without first spelling out the name and because the structure of the claimed polynucleotide is not clearly set forth. For examination purposes, claim 36 will be interpreted to be drawn to a polynucleotide which encodes a polypeptide consisting of amino acids 1-230 of SEQ ID NO: 2 and the amino acid sequence of an hemophilus haemagglutinin (HA) tag, wherein the HA tag is linked to amino acid 230 of SEQ ID NO: 2.

Claim 38 is drawn to a nucleic acid which encodes a “naturally occurring polypeptide”. It is not clear what biological function or polypeptide structure is meant by a “naturally occurring polypeptide”. Thus, the phrase “naturally occurring polypeptide” does not provide adequate metes and bounds for the claimed polynucleotides.

9. Claims 9, 23-26, 28, 35, 36 and 38-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 23-26, 28, 35 and 36 each encompass a genus of polynucleotides which may vary significantly in structure from the polynucleotide sequence of SEQ ID NO: 1 or any polynucleotide that is a coding sequence for the amino acid sequence of SEQ ID NO: 2. Claim 9 encompasses any host cell that comprises the nucleic acids of claim 2, 23 or 24.

Claims 38-40 are broadly drawn to isolated, enriched or purified nucleic acid molecules which encode naturally occurring polypeptides and which hybridize to the nucleic acid molecule as defined in claim 2. Claims 38-40 are interpreted to be drawn to a genus of polynucleotides of varying size and encoding polypeptides of any biological function. Because the claim does not specify that claimed species only includes those nucleic acids which hybridize over the entire length of a polynucleotide encoding SEQ ID NO: 2, claims 38-40 include polynucleotide species that vary considerably in structure and function from that of polynucleotides consisting of a coding sequence for the amino acid sequence of SEQ ID NO: 2.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art, as of the filing date sought, that he or she was in possession of the invention. The invention, for purposes of the ‘written description’ inquiry, is whatever is now claimed.” (See page 1117). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). The specification discloses SEQ ID NO: 1 a polynucleotide sequence encoding SEQ ID NO: 2 which is the amino acid sequence of a receptor Type I serine/threonine kinase. In the instant case, claims 23-26, 28, 35 and 36 are each drawn to a genus of polynucleotides which comprise nucleic acids encoding portions of SEQ ID NO: 2. Because of the open language, the claims are drawn to polynucleotides which may vary considerably from the disclosed polynucleotides of SEQ ID NO: 1 and from the nucleotides consisting of a coding sequence for SEQ ID NO: 2.

In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that “An adequate written description of a DNA...’requires a precise definition, such as by structure, formula, chemical name, or physical properties’, not a mere wish or plan for obtaining the claimed chemical invention”.

Because the claimed polynucleotides vary considerably in structure and because polynucleotide products are used to make polypeptide products, it stands to reason that the claimed polynucleotides will encode polypeptide products which vary considerably in structure. It is well known that even small changes in the primary sequence of a protein can lead to large changes in protein function (see for example, Lazar, E. et al. Molecular and Cellular Biology, 8(3): 1247-1252, 1988 and Burgess, W.H. et al. J. Cell Biology 111: 2129-2138, 1990) which leads to the highly unpredictable nature of protein chemistry. Without a reasonable ability to predict the function of the encoded protein products, the skilled artisan cannot envision the many protein products encoded by the claimed polynucleotides. Therefore, conception of the claimed polynucleotide molecules is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation of the claimed polynucleotides. Adequate written description of a genus of polynucleotides requires more than a mere statement that the

encompassed species are part of the invention. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

10. Claims 2-5, 9 and 23-40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility.

Independent claims 2, 23, 24, 35 and 37 are drawn to polynucleotides encoding the protein of SEQ ID NO: 2, encoding specified domains of the protein of SEQ ID NO: 2, encoding truncated, signaling incompetent protein of SEQ ID NO: 2 or constitutively active protein of SEQ ID NO: 2. SEQ ID NO: 2 is the amino acid sequence of human ALK-7, a Type I receptor serine/threonine kinase. Independent claim 27 is drawn to a polynucleotide of SEQ ID NO: 1 which is a polynucleotide encoding the amino acid sequence of SEQ ID NO: 2.

Dependent claims 5 and 29-34 are drawn to polynucleotides of claim 2 further comprising a vector or a promoter. Dependent claim 9 is drawn to a host cell comprising the polynucleotides of 2, 23 or 24. Dependent claims 25-28, from 2, 23 or 24, are drawn to fusion constructs or polynucleotides comprising restriction endonuclease sites. Dependent claim 36, from 35, is drawn to a polynucleotide encoding a truncated and signaling incompetent protein of SEQ ID NO: 2 and further comprises an HA tag.

Claims 38-40 are drawn to nucleic acid molecules which encode naturally occurring polypeptides and which hybridize under specified conditions to the nucleic acid molecule as defined in claim 2.

For claims to be supported by a utility under 35 U.S.C. 101, the specification must provide an assertion of a utility for the claimed inventions or the specification must describe the claimed inventions in such a way that a well-established utility for the claimed invention is readily apparent to one of skill in the art. In the instant case, the claimed nucleic acids appear to encode a novel protein which belongs to the ALK (activin receptor-like kinase) family. However, for nucleic acids encoding SEQ ID NO: 2 there is no art-established utility because SEQ ID NO: 2 is the amino acid of a novel protein; nor is there an art-established utility for all of the other species of nucleic acid encompassed by the claims. Thus, there does not appear to be a well-established utility for the claimed polynucleotides, host cells and fusion constructs.

The specification provides asserted utilities for the claimed polynucleotides. The specification teaches that the claimed polynucleotides may be used to encode proteins which are asserted as useful for making antibodies; which would be useful in screening methods; or to encoded the kinase domain of ALK-7 to test molecules that would inhibit kinase function. The polynucleotides are also asserted to be useful to make transgenic animals for the study of ALK-7 activity *in vivo*; in gene therapy (the specification fails to indicate any disease which may be treated).

The above asserted utilities are not found to be specific and substantial utilities because the encoded protein, ALK-7, does not have an established biological function or an established association with a disease state. All of the asserted utilities are utilities that may be asserted for any protein, and in the case of testing for compounds which inhibit kinase activity, may be asserted for any kinase. The specification fails to teach specific biological functions of ALK-7 that would make it a useful target for drugs, which drugs may be discovered in a screening method for kinase inhibitors. The specification fails to teach a specific disease state that would endow a gene therapy method employing a polynucleotide encoding an ALK-7 a specific purpose. As for utilities such as that of making antibodies from the encoded protein and that of making transgenic animals from the claimed polynucleotides, the sole purpose of using the claimed inventions in these methods appears to be that of further study of the claimed invention. Thus, the specification appears to offer nothing more than an invitation to experiment.

It is noted that in one embodiment of the invention, the claimed polynucleotide encode a protein which is asserted to have kinase activity. However, the teaching that the encoded polypeptide has kinase activity is not found to be an adequate basis to support an assertion of a specific and substantial utility because the specification also teaches that the encoded polypeptide is that of a Type I receptor serine/threonine kinase. In the art of enzyme function, it is well recognized that a membrane bound enzyme would not necessarily be functional as an enzyme when removed from the membrane environment because such enzymes often require the presence of associated proteins and other membrane bound structures for biological function. Furthermore,

as taught by Wrana et al (Wrana, J. L. et al., *Nature*, 370: 341-347, 1994; cited in the IDS), a Type I receptor kinase requires the association of a specific Type II receptor kinase to acquire the ability to signal downstream substrates because Type I receptor kinases do not have the ability to bind to any ligand. The specification fails to teach the necessary receptor Type II serine/threonine kinase.

In summary, the various asserted utilities of the claimed polynucleotides are not specific and substantial utilities without further research to identify the physiological function of the encoded kinase, the physiological ligand or the Type II receptor kinase necessary for the function of the polypeptides encoded by the claimed polynucleotides. See *Brenner v. Manson*, 383 U.S. 519, 535-536, 148 USPQ 689, 696 (1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." See also the Revised Interim Utility Guidelines available at www.uspto.gov.

11. Claims 2-5, 9 and 23-40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

12. Claims 38-40 are rejected under 35 U.S.C. 102(e) as being anticipated by either US Patent 5,614,609 ("Ibanez et al., '609" filed 15 Nov 1994), US Patent 5,789,565 ("Ibanez et al., '565"

effective US filing date 15 Nov 1994) or US Patent 5,811,245 (Ibanez et al, '245" effective US filing date 15 Nov 1994).

Claims 38-40 are drawn to polynucleotides which hybridize under stringent conditions to polynucleotides encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2. Ibanez et al., '609, Ibanez et al, '565 or Ibanez et al, '245 disclose an ALK-7 polynucleotide which is almost 98 percent identical in nucleic acid sequence to a polynucleotide encoding SEQ ID NO: 2 (see enclosed sequence alignments). Thus, Ibanez et al disclose a polynucleotide which is the same as that claimed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

AH
Anne L. Holleran
Patent Examiner
January 11, 2001

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